



3 dw

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of : Barbara Enenkel ) Art Unit: To be assigned  
U.S. Appln. No. : 10/724,301 ) Examiner: To be assigned  
Confirmation No. : To be assigned  
U.S. Filing Date : November 26, 2003  
Title of Invention : NEOMYCIN-PHOSPHOTRANSFERASE-GENES AND METHODS  
FOR THE SELECTION OF RECOMBINANT CELLS PRODUCING  
HIGH LEVELS OF A DESIRED GENE PRODUCT  
Attny. Docket No.: 1/1411

Mail Stop Amendment  
Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

July 8, 2004

TRANSMITTAL LETTER FOR INFORMATION DISCLOSURE STATEMENT

Sir:

Transmitted herewith concerning the subject application is an Information Disclosure Statement (Form 1449A/B) under 37 C.F.R. §§1.56 and 1.97, as more specifically described hereinbelow.

☒ 1.97(b). This Statement is being filed: i) within three (3) months of the filing date of a national application other than a continued prosecution application under 37 C.F.R. §1.53 (d); ii) within three (3) months of the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in an international application; iii) before the mailing of a first Office action on the merits; or iv) before the mailing of a first Office action after the filing of a request for continued examination under 37 C.F.R. §1.114.

☐ 1.97(c). This Statement is being filed after the time period specified in 37 C.F.R. §1.97(b), but before the mailing date of: i) a final action under 37 C.F.R. §1.113, ii) a notice of allowance under 37 C.F.R. §1.311, or iii) an action that otherwise closes prosecution in the application. This Statement is being accompanied by:

☐ A statement as specified in 37 C.F.R. §1.97(e) [see below]; or

☐ The fee set forth in 37 C.F.R. §1.17(p).

☐ The Commissioner is hereby authorized to charge payment of the \$180.00 fee set forth in 37 C.F.R. §1.17(p) to Deposit Account No. 02-2955.

☐ 1.97(d). This Statement is being filed after the period specified in 37 C.F.R. §1.97(c) but on or before payment of the issue fee. This Statement is accompanied by a statement as specified in 37 C.F.R. §1.97(e) [see below] and the fee set forth in 37 C.F.R. §1.17(p).

☐ 1.97(e).

☐ Each item of information contained in the instant information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three (3) months prior to the filing of the instant information disclosure statement; or

☐ No item of information contained in the instant information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in the instant information disclosure statement was known to any individual designated in 37 C.F.R. §1.56(c) more than three (3) months prior to the filing of the instant information disclosure statement.

☐ The fee set forth in 37 C.F.R. §1.17(p).

☐ The Commissioner is hereby authorized to charge payment of the \$180.00 fee set forth in 37 C.F.R. §1.17(p) to Deposit Account No. 02-2955.

☐ 1.704(d). Each item of information contained in the accompanying information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, which communication was not received by any individual designated in section 1.56(c) more than thirty (30) days prior to the filing of the accompanying information disclosure statement.

☒ The Commissioner is hereby authorized to charge payment of any additional filing fees required under 37 C.F.R. §1.16 and any patent application processing fees under 37 C.F.R. §1.17, or credit any overpayment of same, to Deposit Account No. 02-2955.

Triplicate copies of this form are enclosed.

Respectfully submitted,



Susan K. Pocchiari  
Attorney for Applicant(s)  
Reg. No. 45,016

Patent Department  
Boehringer Ingelheim Corp.  
900 Ridgebury Road, P.O. Box 368  
Ridgefield, CT 06877  
Tel: (203) 798-5648

Certificate of Mailing

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Mail Stop Amendment  
Commissioner For Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

on July 8, 2004.



Susan K. Pocchiari, Reg. No. 45,016



Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**Complete if Known**

**(Use as many sheets as necessary)**

Sheet

1

of

4

Application Number

10/724.301

Filing Date

November 26, 2003

**First Named Inventor**

Barbara Enenkel

## Art Unit

To be assigned

Examiner Name

**To be assigned**

Attorney Docket Number

1/1411

[illegible]

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> *Number <sup>4</sup> *Kind Code <sup>5</sup> (if known)				
		WO 99/53046	10/21/1999	Chiron Corporation		

Examiner  
Signature

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

***If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.***



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

2

of

4

**Complete if Known**

Application Number	10/724,301
Filing Date	November 26, 2003
First Named Inventor	Barbara Enenkel
Art Unit	To be assigned
Examiner Name	To be assigned
Attorney Docket Number	1/1411

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		J. BLAZQUEZ ET AL; Mutations in the aphA-2 gene of transposon Tn5 mapping within the regions highly conserved in aminoglycoside-phosphotransferases strongly reduce aminoglycoside resistance; Molecular Microbiology (1991) Vol. 5 No. 6 pages 1511-1518; National Library of Medicine	
		PAUL R. THOMPSON ET AL; The COOH Terminus of Aminoglycoside Phosphotransferase (3')-IIla Is Critical for Antibiotic Recognition and Resistance; The Journal of Biological Chemistry Vol. 274 No. 43 pages 30697-30706 (1999); American Soc. for Biochemistry and Molecular Biology, Inc.	
		MARIANNE Z. METZ ET AL; Construction and Characterization of Single-Transcript Tricistronic Retroviral Vectors Using Two Internal Ribosome Entry Sites; Somatic Cell and Molecular Genetics (1998) Vol. 24 No. 1 Pages 53-69; Plenum Publishing Corp.	
		HITOSHI NIWA ET AL; Efficient selection for high-expression transfectants with a novel eukaryotic vector; Gene (1991) Vol. 108 pages 193-200; Elsevier Science Publishers B.V.	
		RICHARD L. YENOFISKY ET AL; A mutant neomycin phosphotransferase II gene reduces the resistance of transformants to antibiotic selection pressure; Biochemistry (May 1990) Vol. 87 pages 3435-3439; Proc. Natl Acad Science	
		WAI-CHING HON ET AL; Structure of an Enzyme Required for Aminoglycoside Antibiotic Resistance Reveals Homology to Eukaryotic Protein Kinases; Cell (June 13, 1997) Vol. 89 pages 887-895; Cell Press	
		CORD HEMANN ET AL; High Copy Expression Vector Based on Amplification-Promoting Sequences; DNA and Cell Biology (1994) Vol. 13 No. 4 pages 437-445; Mary Ann Leibert Inc Publishers	
		ROLF G. WERNER ET AL; Appropriate Mammalian Expression Systems for Biopharmaceuticals; Drug Research (1998) Vol. 48(II) No. 8 pages 870-880; Sonderdruck/ Reprint	
		GAIL URLAUB ET AL; Deletion of the Diploid Dihydrofolate Reductase Locus from Cultured Mammalian Cells; Cell (1983) Vol. 33 pages 405-412; Department of Biological Sciences, Columbia University	
		YOSHIKAZU SUGIMOTO ET AL; Efficient Expression of Drug-selectable Genes in Retroviral Vectors under Control of an Internal Ribosome Entry Site; Bio/Technology (July 1994) Vol. 12 pages 694-698; National Cancer Institute	

Examiner  
SignatureDate  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



PTO/SB/08b (08-03)

Approved for use through 06/30/2006. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

3

of

4

**Complete if Known**

Application Number	10/724,301
Filing Date	November 26, 2003
First Named Inventor	Barbara Enenkel
Art Unit	To be assigned
Examiner Name	To be assigned
Attorney Docket Number	1/1411

**NON PATENT LITERATURE DOCUMENTS**

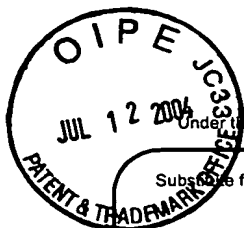
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		K.J. SHAW ET AL; Molecular Genetics of Aminoglycoside Resistance Genes and Familial Relationships of the Aminoglycoside-Modifying Enzymes; Microbiological Reviews (Mar. 1993) Vol. 57 No. 1 pages 138-163; American Society for Microbiology	
		N. RAMESH ET AL; High-titer bicistronic retroviral vectors employing foot-and-mouth disease virus internal ribosome entry site; Nucleic Acids Research (1996) Vol. 24 No. 14 pages 2697-2700; Oxford University Press	
		JERRY PELLETIER ET AL; Internal initiation of translation of eukaryotic mRNA directed by a sequence derived from poliovirus RNA; Nature (July 1998) Vol. 334 pages 320-325; McGill Cancer Center, McGill University, Montreal Canada	
		D.D. MOSSER ET AL; Use of a Dicistronic Expression Cassette Encoding the Green Fluorescent Protein for the Screening and selection of Cells Expressing Inducible Gene Products; Biotechniques (January 1997) Vol. 22 pages 150-161; National Research Council, Montreal Canada	
		RICHARD A. MORGAN ET AL; Retroviral vectors containing putative internal ribosome entry sites: development of a polycistronic gene transfer system and applications to human gene therapy; Nucleic Acids Research (1992) Vol. 20 No. 6 pages 1293-1299; Molecular Hematology Branch	
		LUCIA MONACO ET AL; Expression of recombinant human granulocyte colony-stimulating factor in CHO dhfr-cells: new insights into the in vitro amplification expression system; Gene (1996) Vol. 180 pages 145-150; Elsevier Science B.V.	
		RANDAL J. KAUFMAN; Selection and Coamplification of Heterologous Genes in Mammalian Cells; Methods in Enzymology (1990) Vol. 185 Pages 537-566; Academic Press	
		SUNG K. JANG ET AL; Initiation of Protein Synthesis by Internal Entry of Ribosomes into the 5' Nontranslated Region of Encephalomyocarditis Virus RNA In Vivo; Journal of Virology (April 1989) Vol. 63 No. 4 pages 1651-1660; American Society for Microbiology	
		KEITH D. HANSON ET AL; Analysis of Biological Selections for High-Efficiency Gene Targeting; Molecular and Cellular Biology (Jan. 1995) Vol. 15 No. 1 pages 45-51; American Society for Microbiology	
		MARTIN CHALFIE ET AL; Green Fluorescent Protein as a Marker for Gene Expression; Science (February 11, 1994) Vol. 263 pages 802-805;	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

4

of

4

**Complete if Known**

Application Number	10/724,301
Filing Date	November 26, 2003
First Named Inventor	Barbara Enenkel
Art Unit	To be assigned
Examiner Name	To be assigned
Attorney Docket Number	1/1411

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		MONIQUE V. DAVIES ET AL; The Sequence Context of the Initiation Codon in the Encephalomyocarditis Virus Leader Modulates Efficiency of Internal Translation Initiation; Journal of Virology April 1992 Vol. 66 No. 4 pages 1924-1932; American Society for Microbiology	
		D.L. BURK ET AL; Structural Analyses of Nucleotide Binding to an Aminoglycoside Phosphotransferase; Biochemistry 2001 Vol. 40 pages 8756-8764; American Chemical Society	
		ROBERT P. BENNETT ET AL; Fusion of Green Fluorescent Protein with the Zeocin TM-Resistance Marker Allows Visual Screening and Drug Selection of Transfected Eukaryotic Cells; Biotechniques March 1998 Vol. 24 No. 3 pages 478-482; Invitrogen Corporation Carlsbad, Ca	
		MOHAMMAED A ADAM ET AL; Internal Initiation of Translation in Retroviral Vectors Carrying Picornavirus 5' Nontranslated Regions; Journal of Virology September 1991 Vol. 65 No. 9 pages 4985-4990; American Society for Microbiology	
		WAI-CHING HON ET AL; Structure of an Enzyme Required for Aminoglycoside Antibiotic Resistance Reveals Homology to Eukaryotic Protein Kinases; Cell June 13, 1997 Vol. 89 pages 887-895; Cell Press	
		RICHARD L. YENOFISKY ET AL; A Mutant neomycin phosphotransferase II gene reduces the resistance of transformants to antibiotic selection pressure; Pro. Natl Acad. Science May 1990 Vol. 87 pages 3435-3439; Phytogen Pasadena, CA	
		SEMRA KOCABIYIK ET AL; Site-Specific Mutations of Conserved C-Terminal Residues in Aminoglycoside 3'-Phosphotransferase II: Phenotypic and Structural Analysis of Mutant Enzymes; Biochemical and Biophysical Research Comm. June 1992 Vol. 185 No. 3 pages 925-931; Academic	
		J. BLAZQUEZ ET AL; Mutations in the aphA-2 gene of transposon Tn5 mapping within the regions highly conserved in aminoglycoside-phosphotransferases strongly reduce aminoglycoside resistance; Molecular Microbiology 1991 Vol. 5 No. 6 pages 1511-1518	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.